(iv) performing protein threading on one or more protein encoded by the selected recombinant sequence, or a protein encoded by one or more of the parental nucleic acids; and,

(v) selecting the cross-over sites for recombination between the sequences of two or more parental nucleic acids to occur within regions of structural overlap;

(vi) performing one or more of: PDA, a branch-and-terminate combinatorial optimization analysis, a dead end elimination, a genetic or mean-field analysis, or an analysis of protein folding by threading, of the selected recombinant sequence or of a protein encoded by the selected recombinant sequence;

(vii) performing PDA of at least one protein encoded by at least one of the parental nucleic acids; or

comparing a PDA model of a protein encoded by the selected recombinant sequence to a PDA model of a protein encoded by at least one of the two or more parental nucleic acids.

REMARKS AND RESPONSE TO RESTRICTION

With this amendment and response to restriction, claims 1-46 and 93-98 are pending. The above amendments merely clarify the language of the claims and are fully supported by the specification and original claims as filed. No new matter is introduced by the amendments. Furthermore, the amendments are not made for reasons of patentability and Applicants note that the scope of the claims under the doctrine of equivalents or otherwise is not intended to be limited by the amendments.

RESPONSE TO RESTRICTION

In response to the restriction requirement mailed December 7, 2000, Applicants elect Group I (claims 1-46 and 93-98) without traverse.

With respect to the election of species requirement for claim 6, Applicants elect "a cross-over between any one of the one or more parental character strings or one or more character string subsequences or an additional character string."

NOTIFICATION OF ADDITIONAL RELATED PENDING APPLICATIONS

Applicants note that there are several pending applications related to the present application. These include: USSN 09/494,282 filed January 18, 2000, USSN 09/484,850 filed January 18, 2000, PCT/US00/01202 filed January 18, 2000, PCT/US00/01203 filed January 18, 2000, PCT/US00/01138 filed January 18, 2000, USSN 09/408,392 filed September 28, 1999, USSN 09/416,375 filed October 12, 1999, USSN 09/416,837 filed October 12, 1999 and USSN 09/408,393 filed September 28, 1999, USSN 09/626,588 filed July 27, 2000, USSN 09/626,930 filed July 27, 2000, USSN 09/626,595 filed July 27, 2000, USSN 09/626,929 filed July 27, 2000, USSN 09/626,601 filed July 27, 2000, USSN 09/694,863 filed October 23, 2000, USSN 09/694,864 filed October 23, 2000, USSN 09/721,601 filed November 21, 2000, USSN 09/618,579 filed July 18, 2000, USSN 09/721,396 filed November 21, 2000, USSN 09/721,395 filed November 21, 2000, USSN 09/721,598 filed November 21, 2000, USSN 09/718,765 filed November 21, 2000, USSN 09/718,849 filed November 21, 2000, USSN 09/718,682 filed November 21, 2000 and 09/721,365 filed November 21, 2000.

An information disclosure statement citing these applications and copies of the applications are being sent under separate cover.

CONCLUSION

Applicants believe that this preliminary amendment and response to restriction is fully responsive. Please contact the undersigned with any questions regarding the application or if a telephone conference would expedite consideration of the application.

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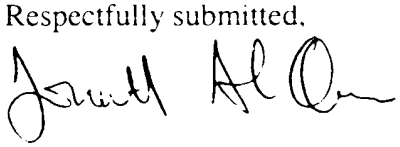
Respectfully submitted,



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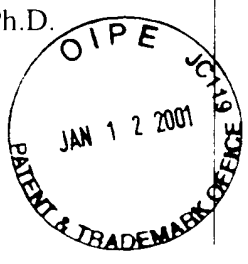

Marked Copy of Amended Claims

9. The method of claim 8, wherein the two or more parental [sequences] **character strings** display low sequence similarity.

10. The method of claim 8, further comprising determining [one or more] **a** sequence for one or more putative recombinant nucleic acid**s** resulting from in silico recombination of the two or more parental [sequences] **character strings** at the cross-over sites, and performing one or more in silico simulation of activity for [the] one or more **of the** putative recombinant nucleic acid**s, or for a protein encoded by one or more of the putative recombinant nucleic acids**.

21. The method of claim 1, wherein the set of oligonucleotides is provided by synthesizing the oligonucleotides to comprise one or more modified parental character string subsequence**s**, which subsequence**s** comprises one or more of:

a parental character string subsequence modified by one or more replacement of one or more character of the parental character string subsequence with one or more different character;

a parental character string subsequence modified by one or more deletion or insertion of one or more characters of the parental character string subsequence;

a parental character string subsequence modified by inclusion of a degenerate sequence character at one or more randomly or non-randomly selected positions;

a parental character string subsequence modified by inclusion of a character string from a different character string from a second parental character string subsequence at one or more position;

a parental character string subsequence which is biased based upon its frequency in a selected library of nucleic acids; and,

a parental character string subsequence which comprises**, or encodes a polypeptide that comprises,** one or more sequence motif, which sequence motif is artificially included in the subsequence.

25. The method of claim 1, wherein the [one or more] **plurality of** parental character string**s** comprises at least two parental character strings, wherein the oligonucleotide set comprises at least one oligonucleotide member comprising a chimeric nucleic acid sequence **that comprises a subsequence from each of** [, the at least one oligonucleotide member comprising at least two oligonucleotide member subsequences, wherein the at least two oligonucleotide member subsequences correspond to at least two subsequences from the] at least two parental character strings, **wherein** the [at least two oligonucleotide member] subsequences **from each parental character string are** [being] separated by a crossover point.

26. The method of claim 25, wherein the crossover point is selected by [identifying a plurality of parental character substrings from a plurality of the at least two parental character strings,] aligning **at least one substring of each of at least two of the parental character strings** [the substrings] to display pairwise identity between the substrings, and selecting a point within the aligned sequence as the crossover point.

34. The method of claim 1, further comprising denaturing the recombinant nucleic acid, and contacting the recombinant nucleic acid with at least one additional nucleic acid produced by cleavage of [a] **at least one** parental nucleic acid [encoded by the at least one parental character string].

35. The method of claim 1, further comprising denaturing the recombinant nucleic acid, and contacting the recombinant nucleic acid with at least one additional nucleic acid produced by cleavage of a parental nucleic acid [encoded by the at least one parental character string], which parental nucleic acid is cleaved by one or more of: chemical cleavage, cleavage with a DNAse, and cleavage with a restriction endonuclease.

36. The method of claim 1, wherein **at least one** [the] parental [character string encodes one or more] nucleic acid **encodes one or more proteins** [corresponding to one or more or protein or gene] selected from: EPO, insulin, a peptide hormone, a cytokine, epidermal growth factor, fibroblast growth factor, hepatocyte

growth factor, insulin-like growth factor, an interferon, an interleukins, a keratinocyte growth factor, a leukemia inhibitory factor, oncostatin M, PD-ECSF, PDGF, pleiotropin, SCF, c-kit ligand, **VEGF** [VEGEF], G-CSF, an oncogene **product**, a tumor suppressor, a steroid hormone receptor, a plant hormone, a disease resistance gene **product**, an herbicide resistance gene **product**, a bacterial gene **product**, a monooxygenases[s], a protease, a nuclease, and a lipase.

93. A method of producing recombinant nucleic acids, the method comprising:

providing two or more parental nucleic acid**s** [sequences];

selecting cross-over sites for recombination between the **sequences of the** two or more parental nucleic acid**s** [sequences], thereby defining **sequences of** one or more recombinant nucleic acids that result from a cross-over between at least two of the [two or more] parental nucleic acids;

[determining a recombinant sequence for at least one of the one or more recombinant nucleic acids;]

selecting **a sequence of** [the] at least one recombinant sequence in silico for one or more expected activity; and,

synthesizing **a recombinant nucleic acid corresponding to one or more of the selected** [the at least one] recombinant sequence**s**.

95. The method of claim 94, wherein synthesizing the [at least one] recombinant **nucleic acid** [sequence] comprises providing fragments of [the] two or more **of the** parental nucleic acids and at least one of corresponding bridge oligonucleotides, hybridizing the fragments and the bridge oligonucleotides and elongating the hybridized fragments with a polymerase or a ligase.

96. The method of claim 93, wherein the **sequences of the** two or more parental sequences display low sequence similarity.

97. The method of claim 93, wherein selecting the at least one recombinant sequence in silico comprises one or more of:

(i) performing an energy minimization analysis of **a protein encoded by** the [at least one] **selected** recombinant sequence;

(ii) performing a stability analysis of the at least one **protein encoded by the selected** recombinant sequence;

(iii) comparing an energy minimized model of [the] at least one **protein encoded by the selected** recombinant sequence to an energy minimized model of **a protein encoded by** one or more of the [two or more] parental nucleic acids;

(iv) performing protein threading on one or more [encoded] protein **encoded by the selected recombinant sequence**; and,

(v) selecting the cross-over sites for recombination between the **sequences of** two or more parental nucleic acid sequences to occur within regions of structural overlap[, thereby determining the sequence of the at least one recombinant nucleic acid];

(vi) performing one or more of: PDA, a branch-and-terminate [a] combinatorial optimization analysis, a dead end elimination, a genetic or mean-field analysis, or analysis of protein folding by threading, of the **selected** [at least one] recombinant sequence **or of a protein encoded by the selected recombinant sequence**;

(vii) performing PDA **model** of at least one **protein encoded by at least one** of the [two or more] parental **nucleic acids** [sequences]; or

(viii) comparing a PDA **model** of **a protein encoded by** the [at least one] **selected** recombinant sequence to a PDA **model** of **a protein encoded by** at least one of the two or more parental **nucleic acids** [sequences].